Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
C1-A0305P		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/004696	31.03.2004	31.03.2003

International Patent Classification (IPC) or national classification and IPC

Applicant

CHUGAI SEIYAKU KABUSHIKI KAISHA

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 10 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. 1 and the Supplemental Box.
   b. ☒ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      1 disk , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☒ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☒ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☒ neither restricted the claims nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
   - ☐ complied with.
   - ☒ not complied with for the following reasons:

Degraded antibodies that are capable of recognizing CD22, which are the only feature that is common to claims 1 to 13, can be considered to have been well-known (if necessary, refer to the document WO 98/42378 or the like); therefore, the abovementioned common feature cannot be considered to be a special technical feature. Such being the case, the inventions that are set forth in claims 1 to 13 cannot be considered to be so linked as to form a single general inventive concept.

[Refer to the Supplemental Box]

4. Consequently, this report has been established in respect of the following parts of the international application:
   - ☐ all parts.
   - ☒ the parts relating to claims Nos. 1-13, SEQ ID NO: 1

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	3	YES
	Claims	1, 2, 4-13	NO
Inventive step (IS)	Claims		YES
	Claims	1-13	NO
Industrial applicability (IA)	Claims	1-13	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents are cited in the international search report.

Document 1: WO 01/97858 A2 (IDEC Pharmaceuticals Corp.), 27 December 2001

Document 2: WO 02/22212 A2 (IDEC Pharmaceuticals Corp.), 21 March 2002

Document 3: WO 01/74388 A1 (IDEC Pharmaceuticals Corp.), 11 October 2001

Document 4: WO 02/04021 A1 (IDEC Pharmaceuticals Corp.), 17 January 2002

Document 5: JP 2001-518930 A (Immunomedics, Inc.), 16 October 2001

Document 6: JP 2002-544173 A (Immunomedics, Inc.), 24 December 2002

Document 7: JP 10-505231 A (Immunomedics, Inc.), 26 May 1998

Document 8: P. HOLLIGER et al., "'Diabodies': small bivalent and bispecific antibody fragments," Proc. Natl. Acad. Sci. USA., 1993, No. 90, Vol. 14, p. 6444 to 6448

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The inventions set forth in claims 1, 2 and 4 to 13 lack novelty and do not involve an inventive step in the light of documents 1 to 4.

Documents 1 to 4 all indicate that fragments from anti-CD22 antibodies exhibit an activity whereby they induce apoptosis in tumor cells such as lymphoma cells or leukaemic cells, and further present diabodies as examples of said fragments. Therein, the anti-CD22 antibodies that are employed in the examples of document 1 can be considered to be LL2 antibodies.

The inventions set forth in claims 1, 4 and 6 to 11 lack novelty and do not involve an inventive step in the light of documents 5 and 6.

Documents 5 and 6 both indicate that fragments from anti-CD22 antibodies are effective for the treatment of tumors that are caused by lymphoma, leukaemia or the like, and further present sFv proteins and the like as examples of said fragments. In addition, documents 5 and 6 present LL2 antibodies as examples of said anti-CD22 antibodies.

Therein, it is thought that the antibody fragments disclosed in documents 5 and 6 exhibit a therapeutic effect in relation to tumors because they induce apoptosis in cancer cells.

The inventions set forth in claims 1, 4 and 6 to 11 lack novelty and do not involve an inventive step in the light of document 7.

Document 7 indicates that fragments of LL2 monoclonal antibodies, which are anti-CD22 antibodies, are effective for the treatment of tumors that are caused by lymphoma, leukaemia or the like.

Therein, it is thought that the antibody fragments

disclosed in document 7 exhibit a therapeutic effect in relation to tumors because they induce apoptosis in cancer cells.

The invention set forth in claim 3 does not involve an inventive step in the light of documents 1 to 4 and documents 7 and 8.

Document 7 discloses the base sequence of the variable region in LL2 monoclonal antibodies.

Document 8 discloses a method for the preparation of diabodies, and also makes disclosures in relation to the feature of appending a linker sequence or a peptide tag.

As a result, it would be easy for a person skilled in the art to conceive of employing the base sequence for LL2 monoclonal antibodies that is disclosed in document 7 and the method for the preparation of diabodies that is disclosed in document 8 when preparing diabodies from the LL2 monoclonal antibodies that are disclosed in documents 1 to 4.

The inventions set forth in claims 2, 3, 5, 12 and 13 do not involve an inventive step in the light of documents 5 and 6 and documents 7 and 8.

It is thought that diabodies were known to be one type of antibody fragment at the time the present application was filed.

As a result, the antibody fragments that are disclosed in documents 5 and 6 include diabodies; therefore, it would be easy for a person skilled in the art to conceive of employing the base sequence for LL2 monoclonal antibodies that is disclosed in document 7 and the method for the preparation of diabodies that is disclosed in document 8 when preparing said fragments

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

(diabodies).

The inventions set forth in claims 2, 3, 5, 12 and 13 do not involve an inventive step in the light of documents 7 and 8.

It is thought that diabodies were known to be one type of antibody fragment at the time the present application was filed.

As a result, the antibody fragments that are disclosed in document 7 include diabodies; therefore, it would be easy for a person skilled in the art to conceive of employing the base sequence for LL2 monoclonal antibodies that is disclosed in document 7 and the method for the preparation of diabodies that is disclosed in document 8 when preparing said fragments (diabodies).

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Box No. VI **Certain documents cited**

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/*month*/*year*)	Filing date (day/*month*/*year*)	Priority date (valid claim) (*day*/month/*year*)
WO 03/33654 A2 (E,X)	24.04.2003	15.10.2002	15.10.2001

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/*month*/*year*)	Date of written disclosure referring to non-written disclosure (*day*/month/*year*)

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, Item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☐ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

Box IV

As a result, the inventions that are set forth in claims 1 to 13 can be classified into four groups of inventions, as follows: (1) degraded antibodies which have the amino acid sequence that is set forth in SEQ ID NO: 1; (2) degraded antibodies which have the amino acid sequence that is set forth in SEQ ID NO: 3; (3) degraded antibodies which have the amino acid sequence of the CDR of SEQ ID NO: 5 or the CDR of SEQ ID NO: 7; and (4) degraded antibodies which have the amino acid sequence of the CDR of SEQ ID NO: 9 or the CDR of SEQ ID NO: 11.